

Claims

1. A process for the manufacture of 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, and optionally therefrom tocopheryl acetate, which comprises either

5 (a) C-alkylating 2,3,6-trimethylhydroquinone-1-acetate with isophytol or phytol in the presence of a sulphur(VI) containing catalyst of the formula R^1SO_2OH , wherein R^1 signifies hydroxy, halogen, lower alkyl, halogenated lower alkyl or aryl, in an aprotic organic solvent, or

(b) O-alkylating 2,3,6-trimethylhydroquinone-1-acetate with a phytyl halide in a polar aprotic organic solvent in the presence of a base, and subjecting the so-obtained 4-O-
10 phytyl-2,3,6-trimethylhydroquinone-1-acetate to a rearrangement reaction,

and in each case optionally submitting the so-obtained 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate to a ring closure reaction to produce tocopheryl acetate.

2. A process according to claim 1 for the manufacture of 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, which comprises C-alkylating 2,3,6-
15 trimethylhydroquinone-1-acetate with isophytol or phytol in the presence of a sulphur(VI) containing catalyst of the formula R^1SO_2OH , wherein R^1 signifies hydroxy, halogen, lower alkyl, halogenated lower alkyl or aryl, in an aprotic organic solvent.

3. A process according to claim 1 for the manufacture of 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, which comprises O-alkylating 2,3,6-
20 trimethylhydroquinone-1-acetate with a phytyl halide in a polar aprotic organic solvent in the presence of a base, and subjecting the so-obtained 4-O-phytyl-2,3,6-trimethylhydroquinone-1-acetate to a rearrangement reaction.

4. A process for the manufacture of tocopheryl acetate, which comprises submitting 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate or an isomer thereof, namely (Z)-4-
25 hydroxy-2,3,6-trimethyl-5-(3,7,11,15-tetramethylhexadec-3-enyl)-phenyl acetate, (E)-4-hydroxy-2,3,6-trimethyl-5-(3,7,11,15-tetramethylhexadec-3-enyl)-phenyl acetate or 4-hydroxy-2,3,6-trimethyl-5-[3-(4,8,12-trimethyltridecyl)-but-3-enyl]-phenyl acetate, to a ring closure reaction by treating said acetate with an acidic catalyst in the presence or absence of a solvent.

30 5. A process according to claim 1 for the manufacture of tocopheryl acetate, which comprises C-alkylating 2,3,6-trimethylhydroquinone-1-acetate with isophytol or phytol in the presence of a sulphur(VI) containing catalyst of the formula R^1SO_2OH , wherein R^1

signifies hydroxy, halogen, lower alkyl, halogenated lower alkyl or aryl, in an aprotic organic solvent, and submitting the so-obtained 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate to a ring closure reaction by treating it with an acidic catalyst in the presence or absence of a solvent to produce the tocopheryl acetate.

5 6. A process according to claim 1 for the manufacture of tocopheryl acetate, which comprises O-alkylating 2,3,6-trimethylhydroquinone-1-acetate with a phytol halide in a polar aprotic organic solvent in the presence of a base, subjecting the so-obtained 4-O-phytyl-2,3,6-trimethylhydroquinone-1-acetate to a rearrangement reaction, and
10 submitting the so-obtained 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate to a ring closure reaction by treating it with an acidic catalyst in the presence or absence of a solvent to produce tocopheryl acetate.

7. A process according to any one of claims 1, 2 and 5, wherein the sulphur(VI) containing catalyst of the formula R^1SO_2OH used in the C-alkylation is sulphuric acid, fluorosulphonic acid, methane- or ethane-sulphonic acid, trifluoromethanesulphonic acid
15 or benzene- or p-toluenesulphonic acid, preferably trifluoromethanesulphonic acid or p-toluenesulphonic acid.

8. A process according to any one of claims 1, 2, 5 and 7, wherein the aprotic organic solvent used in the C-alkylation is a polar aprotic organic solvent, particularly an aliphatic or cyclic ketone, e.g. diethyl ketone, isobutyl methyl ketone, cyclopentanone or
20 isophorone; an aliphatic or cyclic ester, e.g. ethyl acetate, isopropyl acetate or γ -butyrolactone; or a dialkyl or alkylene carbonate, e.g. dimethyl carbonate, diethyl carbonate, ethylene carbonate or propylene carbonate; or is a non-polar aprotic organic solvent, particularly an aliphatic hydrocarbon, e.g. hexane, heptane or octane; or an aromatic hydrocarbon, e.g. benzene, toluene or an xylene, or is a biphasic solvent system
25 containing both kinds of aprotic organic solvents, preferably ethylene and/or propylene carbonate as the polar aprotic organic solvent and hexane, heptane or octane as the non-polar aprotic organic solvent.

9. A process according to any one of claims 1, 2, 5, 7 and 8, wherein the sulphur(VI) containing catalyst of the formula R^1SO_2OH used in the C-alkylation is present in an
30 amount of from about 0.01 mol.% to about 1 mol.%, preferably in an amount of about 0.05 mol.% to about 0.1 mol.%, based on the molar amount of phytol or isophytol, whichever is employed.

10. A process according to any one of claims 1, 2 and 5 to 8, wherein the C-alkylation is effected at temperatures from about 20°C to about 160°C, preferably from about 80°C to about 150°C, and most preferably from about 100°C to about 127°C.

11. A process according to any one of claims 1, 3 and 6, wherein the phytyl halide
5 used in the O-alkylation is phytyl bromide or phytyl chloride, preferably phytyl bromide.

12. A process according to any one of claims 1, 3, 6 and 11, wherein the base used in the O-alkylation is sodium hydride.

13. A process according to any one of claims 1, 3, 6, 11 and 12, wherein the aprotic organic solvent used in the O-alkylation is a polar aprotic organic solvent, particularly an
10 aliphatic or cyclic ketone, e.g. diethyl ketone, isobutyl methyl ketone, cyclopentanone or isophorone; an aliphatic or cyclic ester, e.g. ethyl acetate, isopropyl acetate or γ -butyrolactone; a dialkyl or alkylene carbonate, e.g. dimethyl carbonate, diethyl carbonate, ethylene carbonate or propylene carbonate; or a dialkylformamide, e.g. dimethylformamide or dibutylformamide.

14. A process according to any one of claims 1, 3, 6 and 11 to 13, wherein the base
15 for the O-alkylation is used in excess relative to the amount of 2,3,6-trimethylhydroquinone-1-acetate, in particular in a molar excess of about 5 to about 30%, preferably about 10 to about 20%.

15. A process according to any one of claims 1, 3, 6 and 11 to 14, wherein the O-
20 alkylation is effected at temperatures from about -20°C to about +30°C, preferably from about -10°C to about +15°C, and most preferably from about 100°C to about 127°C.

16. A process according to any one of claims 1, 3, 6 and 11 to 15, wherein the
25 rearrangement reaction following the O-alkylation is suitably performed in the presence of an acidic catalyst, in particular a Friedel-Crafts catalyst such as boron trifluoride etherate, in an aprotic organic solvent and at temperatures below about 20°C.

17. A process according to claim 16, wherein the aprotic organic solvent is an alkane, e.g. hexane; a halogenated alkane, e.g. carbon tetrachloride; or a mixtures of these two types of aprotic organic solvents, e.g. a mixture of hexane and carbon tetrachloride.

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18. A process according to claim 16 or claim 17, wherein the rearrangement reaction is performed at temperatures from about -28°C to about -23°C.

19. A process according to any one of claims 1, 4 to 6, wherein the ring closure is effected by treating said acetate with an acidic catalyst which is a sulphur(VI) containing catalyst of the formula R^1SO_2OH wherein R^1 signifies hydroxy, halogen, lower alkyl, halogenated lower alkyl or aryl, particularly sulphuric acid, fluorosulphonic acid, methane- or ethane-sulphonic acid, trifluoromethanesulphonic acid or benzene- or p-toluenesulphonic acid, preferably trifluoromethanesulphonic acid or p-toluenesulphonic acid.

20. A process according to any one of claims 1, 4 to 6 and 19, wherein the ring closure is effected in a polar aprotic organic solvent, particularly an aliphatic or cyclic ketone, e.g. diethyl ketone, isobutyl methyl ketone, cyclopentanone or isophorone; an aliphatic or cyclic ester, e.g. ethyl acetate, isopropyl acetate or γ -butyrolactone; or a dialkyl or alkylene carbonate, e.g. dimethyl carbonate, diethyl carbonate, ethylene carbonate or propylene carbonate.

21. A process according to any one of claims 1, 4 to 6, 19 and 20, wherein the catalyst used in the ring closure is present in an amount of from about 0.01 mol.% to about 10 mol.%, preferably in an amount of about 0.1 to about 5 mol.%, based on the molar amount of the 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate.

22. A process according to any one of claims 1, 3, 6 and 11 to 14, wherein the ring closure reaction is effected at temperatures from about 20°C to about 160°C, preferably from about 80°C to about 140°C.

23. The compound 3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, including each of its stereoisomers (E,all-rac)-3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, (Z,all-rac)-3-phytyl-2,5,6-trimethylhydroquinone-1-acetate, (E,R,R)-3-phytyl-2,5,6-trimethylhydroquinone-1-acetate and (Z,R,R)-3-phytyl-2,5,6-trimethylhydroquinone-1-acetate.

24. The compound 4-hydroxy-2,3,6-trimethyl-5-[3-(4,8,12-trimethyltridecyl)-but-3-enyl]phenyl acetate.